wherein the peptides are randomly or substantially homogeneously distributed over the solid support (see page 12, lines 16-20 of the specification).

Advantages of Applicants' Invention

Applicants' SAMs that contain peptides bound to a surface in a predetermined pattern allow targets, such as cells of a specific type, which bind to the peptides to be assembled at a particular locus on a surface (see page 2, lines 21-33 of the specification). The ability to assemble target cells in a predetermined pattern on a surface can be useful in assays such as drug screening assays, as well as, studies involving the formation of connections between cells, such as neurons (see page 21, line 3 to page 22, line 8 of the specification).

In addition, Applicants' SAMs are more readily assembled than prior art monolayers prepared using peptides because peptides are bound directly to the solid support via a terminal amino acid. Therefore, standard peptide synthesis techniques can be used to prepare the peptides.

Claim Amendments

Applicants have amended Claims 1 and 17-19 to make clear that a predetermined pattern refers to ordered areas where peptides are bound or not bound on the solid support. The amendment to the claims also makes clear that the composition of matter claimed does not include peptides which are randomly or substantially homogeneously distributed on a solid support. Support for these amendments can be found on page 12, lines 12-20 of the specification.

Interview Summary

Applicants agree with the Examiner's summary of the interview.

Rejection of Claims 1-17 Under 35 U.S.C. § 102 Over Wang *et al.* (Abstract)

The Examiner rejected Claims 1-17 over Wang *et al.*, *Chem. Abstracts*, vol. 125, no. 257089b (hereinafter "Wang *et al.*") alleging that the reference teaches peptide monolayers of the recited type. Please note that, although the Examiner referred to the reference as Wang *et al.*, the first author on the reference is Chaikof. To avoid confusion, however, Applicants will also refer to the reference hereinafter as "Wang *et al.*" The Examiner did not find Applicants' argument

that the reference does not teach deposition of the monolayer in a predetermined pattern persuasive because the Examiner felt that Wang *et al.* are referring to predetermined order of deposition of monolayers when they state in the abstract that "[w]ell-ordered protein assemblies on metallic substrates can be produced . . ."

Applicants have obtained a copy of the full reference of Wang *et al.*, *Mat. Res. Soc Symp. Proc. 414*:17 (see Exhibit A). Wang *et al.* teach the synthesis of two peptides which are covalently bound to a thioethyl group which can bind to a solid support. The two peptides have the following sequences (wherein "βA" refers to β-alanine):

$GRGD(\beta A)_3Y\text{-}NH(CH_2)_2SH$; and
$(\beta A)_6\text{-}NH(CH_2)_2SH$.

Three peptide monolayers were made by exposing a gold coated surface to a solution of the thioethyl modified peptides (see Exhibit A, p. 18, paragraph 1). The first Monolayer was composed of $GRGD(\beta A)_3Y\text{-}NH(CH_2)_2SH$, the second Monolayer was composed of $(\beta A)_6\text{-}NH(CH_2)_2SH$ and the third Monolayer was composed of a mixture of both peptides. The monolayers of peptides were then characterized by atomic force microscopy.

Monolayers prepared using peptide $(\beta A)_6\text{-}NH(CH_2)_2SH$ alone had a homogeneous, closely packed surface (see Exhibit A, page 19, lines 15-21). The peptide chains aligned in a β-sheet structure. It is this β-sheet structure which the phrase "[w]ell-ordered protein assemblies . . ." refers to in the abstract of Wang *et al.* It does not refer to the distribution of peptides on the surface in a predetermined pattern.

Monolayers prepared using peptide $GRGD(\beta A)_3Y\text{-}NH(CH_2)_2SH$ alone had islands of protein deposits of random size and location (see Exhibit A, page 19, lines 21-23 and Figure 2 on page 20).

Monolayers prepared using a 1:1 mixture of both peptides had surfaces which combined the features of monolayers prepared from each peptide alone (see Exhibit A, p. 19, lines 23-25).

Applicants are not referring to alignment of peptide chains when they describe peptide assemblies in a predetermined pattern. Applicants define "predetermined pattern" on page 12, lines 13-20 of the specification as follows:

> The terms "printed", "patterned" or "predetermined pattern" are defined herein to mean that the solid support has ordered areas

> where the peptides are boned and not bonded to the solid support. That is, a printed or patterned solid support is expressly not intended to include a support with random or substantially homogeneous distribution of the peptide over its entire surface(s).

None of the monolayers prepared by Wang *et al.* have predetermined ordered areas where peptides are bound and not bound on the solid support, as in Applicants' claimed SAMs. Monolayers prepared by Wang *et al.* have either a homogeneous surface or a surface that has randomly distributed protein islands of varying size. These two types of monolayers are specifically excluded from Applicants definition of SAMs having a predetermined pattern. To make this clear that Applicants are not claiming SAMs which have a homogeneous or random distribution of peptides on a solid surface. Applicants have amended the claims to specifically excluded these types of SAMs.

In addition, the method of making peptide monolayers taught by Wang *et al.* would not teach a person skilled in the art how to assemble peptides on a surface in a predetermined pattern. Wang *et al.* make peptide monolayers by contacting a gold coated surface with a solution of a peptide (see page 18, paragraph 1). The solution contacts the surface uniformly so there is no method taught by Wang *et al.* by which the peptides can assemble in a predetermined pattern on the surface.

The peptide monolayers prepared by Wang *et al.* also differ from Applicants' SAMs because the peptides are not bound directly to the solid support. Instead, Wang *et al.* use peptides which have been modified to include a thioethyl group. The thioethyl group binds to the solid support. In Applicants' SAMs, peptides are bound directly to the solid support through a terminal amino acid (see page 3, lines 1-5 of the specification).

The Federal Circuit has determined that

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987).

Two elements of Applicants' claims are not found in Wang *et al.* Applicants' claimed SAMs have a predetermined pattern that has ordered areas where the peptides are bound and not bound. In the peptide monolayers prepared by Wang *et al.*, peptides are distributed either homogeneous or randomly over the solid support. In addition, the peptide monolayers of Wang *et al.* are

constructed with peptides which have been modified to include a covalently bound thioethyl group which can bind to a solid support. Applicants' claimed SAMs are bound directly to a solid support through a terminal amino acid group.

When Wang *et al.* is considered in its entirety, it clearly does not describe every element of Applicants' claimed composition of matter. Therefore, Wang *et al.* do not anticipate Applicants' Claims 1-17, and Applicants respectfully request that the rejection under 35 U.S.C. § 102(a) be reconsidered and withdrawn.

Rejection of Claims 18 and 19 Under 35 U.S.C. § 103(a) Over Wang *et al.* (Abstract) in View of Kumar *et al.*

The Examiner stated in the previous Office Action, paper no. 6, mailed on July 8, 1998 that "Wang *et al.* teach a substrate comprising self assembled monolayers of peptides," and that "[t]he difference between Wang *et al.* and the instant claims is that the reference fails to teach the formation of the monolayers by using a stamp having a predetermined pattern on a substrate and forming the monolayers by a microstamping technique."

The Examiner summarized the teachings of Kumar *et al.* as ". . . a method for the formation of monolayer assembled on solid surfaces using a microstamping techniques. . ." with ". . . a variety of molecular species that can be bonded onto a variety of solid supports . . ." The Examiner interpreted the following sentence in Kumar *et al.* to mean that the molecular species taught by Kumar *et al.* includes peptides:

> Additional suitable functional groups include acid chlorides, anhydrides, sulfonyl groups, phosphoryl groups, hydroxyl groups and amino acid groups. Kumar *et al.*, Col. 10, line 66 to Col. 11, line 1.

The Examiner stated that because Kumar *et al.* teach that their microstamping method can be used to attach a variety of molecular species to a solid substrate, this provides a motivation to combine the reference with Wang *et al.* The Examiner concluded that it would have been obvious to one having ordinary skill in the art at the time of invention to have obtained self-assembled peptide monolayers as taught by Wang *et al.* using a microstamping technique to form the monolayers as suggested by Kumar *et al.*

Wang *et al.* teach a method of forming a peptide monolayers by contacting a gold covered surface with a solution of a peptide. The peptides have been modified to include a

thioethyl group which binds to the solid support. The method of Wang *et al.* differs from Applicants' claimed method in at least two ways. In the method of Wang *et al.*, the peptides are not assembled on a solid support in a predetermined pattern. In addition, in the method of Wang *et al.*, the peptides used to form the monolayers are modified to include a thioethyl group which binds to the solid support. In Applicants' method, peptides are bound directly to the solid support.

Kumar *et al.* teach a microstamping technique wherein a monolayer of a molecular species can be applied to a solid support. The genus of compounds designated "molecular species", which Kumar *et al.* teach, can be used to form SAMs, have a first terminal functional group that can bind to the solid support; a spacer connected to the terminal functional group; and, optionally, a second functional group attached to the spacer that can bind to biological or chemical species (see Kumar *et al.*, Col. 10, lines 23-29). The molecular species taught can be represented by general formula R'-A-R". R' is the terminal functional group, preferably -SH, and is selected to bind to the solid support. A is a spacer, preferably having the formula $-(CH_2)_n-$, where n is from 1-30. The examples which Kumar *et al.* list as suitable spacers are saturated or unsaturated, linear or branched alkyl, aryl, hydrocarbons and their halogenated equivalents (see Kumar *et al.*, Col. 12, paragraph 1). In addition, A is an alkyl linker having from 11 to 16 carbon atoms in all the experimental examples (see Kumar *et al.*, Examples 3-5, Col. 19 and 20). R" is a second functional group which is exposed when the molecular species forms a SAM. R" is preferably $-CH_3$, $-OH$, $-O(CH_2)_nH$, $-CONH(CH_2)_nH$, $-NHCO(CH_2)_nH$, $-(OCH_2CH_2)_nH$ or $-COOH$, where n is 1-15 (see Kumar *et al.*, Col. 12, paragraphs 2 and 3). Kumar *et al.* teach that the first functional group can be an amino acid (see Kumar *et al.*, Col. 10, line 66 to Col. 11, line 1). There is no teaching or suggestion in Kumar *et al.* that the spacer group can be a peptide. In addition, none of the spacer groups listed as preferred embodiments or exemplified by Kumar *et al.* include peptides. Since Kumar *et al.* teach that the molecular species must include at least a first functional group and a spacer, Kumar *et al.* do not teach that the molecular species that is a peptide. Therefore, Applicants' method differs from the method of Kumar *et al.* in the type of molecule which is bound to the solid support in a predetermined pattern.

Applicants' method is non-obvious over the combination of Wang *et al.* and Kumar *et al.*, because there is no suggestion or motivation in either of the references to modify the methods therein to include the teachings of the other reference. M.P.E.P. § 2143.01 states the following:

> The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. (Emphasis in the original.)

Wang *et al.* do not teach or suggest that applying a monolayer of peptides in a predetermined pattern would be desirable. Nor do they disclose a method for doing so. Kumar *et al.* do not teach or suggest that peptides could be used to form SAMs. All of the preferred or exemplified molecular species taught by Kumar *et al.* include long alkyl spacer groups which are more hydrophobic than Applicants' peptides. Since neither reference suggests the desirability of the combination, Applicants' claimed method of preparing SAMs is non-obvious over the combination of Wang *et al.* and Kumar *et al.* Therefore, Applicants respectfully request that the rejection be reconsidered and withdrawn.

SUMMARY AND CONCLUSIONS

Applicants' composition of matter is not anticipated by Wang *et al.* because peptides are not distributed over a solid support in a predetermined pattern in the peptide monolayers prepared by Wang *et al.* In addition, Applicants' claimed method of preparing SAMs is non-obvious over the combination of Wang *et al.* and Kumar *et al.* because neither reference suggests the desirability of combining the teachings of the reference. In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By David C. Brook

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Dated: 8/30/99

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SELF-ASSEMBLING PEPTIDE MONOLAYERS: ENDOTHELIAL CELL BEHAVIOR ON FUNCTIONALIZED METAL SUBSTRATES

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ABSTRACT

Despite the high initial success rate with metallic stents for the treatment of a variety of vascular lesions, problems have included occlusion due to thrombus formation or intimal proliferation. Improving the biological behavior of these and other other implantable metallic devices may require the use of biomimetic peptide coatings which promote specific cellular responses at the biological-materials interface.

Thiol-terminated peptides, without the addition of a cysteine residue, were synthesized by a modification of standard solid phase methodology. Gold/mica or gold/glass surfaces were exposed for 6 hours at 23 °C to one of three peptide solutions: $GRGD(\beta A)_3YNH(CH_2)_2SH$ (RGD); $(\beta A)_6NH\ (CH_2)_2SH$ (bAla); or a 1:1 mix of both peptides. Peptide films were examined by external reflectance infrared (IR) spectroscopy and atomic force microscopy (AFM) which confirmed the presence of unique close-packed structures for bAla and the 1:1 mix. Endothelial cell proliferative, migratory, and adhesive behavior were evaluated using ^{3}H-thymidine and ^{51}Cr labeling techniques, respectively. Cell proliferation, migration, and adhesion were significantly higher on RGD containing peptide films.

Well-ordered protein assemblies on metallic substrates can be produced with the proper choice of peptide chain structure and terminal residues. Biological activity is a function of film composition and oligopeptide pendant structure.

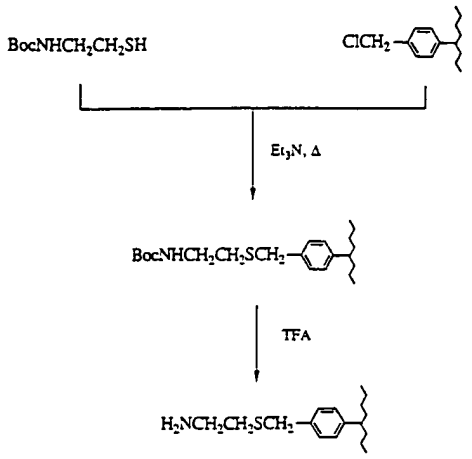
INTRODUCTION

Recent advances in surface engineering have been achieved by following the paradigm of the biological membrane which organizes highly ordered molecular assemblies via processes largely driven by van der Waals attraction forces [1]. Indeed, the stability and order of alkanethiolates on gold, as well as the kinetics of monolayer assembly are enhanced by increasing chain length and associated van der Waals intermolecular interactions. In protein assemblies, nature has provided another well-recognized model system for organizing molecules with intrinsic physiochemical stability which far exceeds that of the cell membrane. These differences are related, in part, to stronger non-covalent interactions mediated by hydrogen bonding, particularly in pleated secondary structures[2]. Here we describe the formation of highly ordered monolayer assemblies driven by hydrogen bond interactions between poly(βalanine) thiolates. By choosing an appropriate peptide pendant or by creating a surface mixture of ligand and non-ligand containing species, biological responses can be controlled.

EXPERIMENTAL METHODS

Peptide Synthesis. Model peptides were synthesized and purified using a solid-phase strategy which has been described in detail elsewhere[3]. Briefly, the synthesis of thiol terminated peptides without the addition of a cysteine residue or the use of other post-synthesis derivatization steps was performed after first derivitizing chloromethylated polystyrene resin with N-t-butoxycarbonyl-2-aminoethanethiol. In this case, after peptide synthesis a free thiol was generated by cleavage of the para-substituted benzyl thioether with hydrogen fluoride (Scheme 1). Two peptides were synthesized: $GRGD(\beta A)_3YNH(CH_2)_2SH$ and $(\beta A)_6NH\ (CH_2)_2SH$.

Mat. Res. Soc. Symp. Proc. Vol. 414 © 1996 Materials Research Society



Scheme 1. Synthetic strategy for preparation of thiol terminated oligopeptides.

Preparation of Peptide Monolayers. Gold substrates were prepared by resistive evaporative deposition of Au metal onto freshly cleaved mica or glass surfaces at the Microelectronic Research Facility at the Georgia Institute of Technology. The epitaxial growth of Au on heated muscovite mica surfaces yields large, atomically flat terraces of primary Au (111) orientation. Au-coated substrates were incubated for 6 hours in 0.1 mM solution containing thiol-terminated oligopeptides in ethanol:water (1:1 v/v). For bioassays, nonspecific serum protein adsorption was reduced by blocking all surfaces by overnight incubation with 1% bovine serum albumin at 4°C.

Surface Analysis. AFM images were obtained with a Digital Instruments (Santa Barbara, CA) NanoScope III atomic force microscope in contact mode. External reflectance IR spectra of films on Au substrates were acquired using a Digilab FTS-40 Fourier transform infrared spectrometer (Bio-Rad, Digilab Division, Cambridge, MA) using p-polarized light at an angle of incidence of 75°. Typically, 1024 scans were coded at 4 cm^{-1} resolution to improve the signal-to-noise ratio.

Cell Culture. Human endothelial cells (ECs) were obtained from umbilical cord veins from the Cell Culture Core Facility, Department of Dermatology, Emory University. The cells were subcultured by a 2-minute incubation in 0.05% trypsin, 0.53 mM EDTA in Hanks Balanced Salt Solution (HBSS; GIBCO, Grand Island, NY), pelleted and resuspended in Medium 199 supplemented with 20% fetal calf serum, 50 µg/mL endothelial mitogen, 80 µg/mL heparin, 2 mM L-glutamine, 100 U/mL penicillin, 100 U/mL streptomycin, and 250 µg/mL fungizon. Migration and proliferation assays were performed in endothelial growth medium (EGM, Clonetics Inc.) which consists of modified MCDB 131 (Clonetics Inc.), 2% fetal bovine serum, 10 ng/mL of human EGF, 1 µg/mL hydrocortisone, 0.4% bovine brain extract, 40 ng/mL heparin, 100 U/mL penicillin, 100 U/mL streptomycin, and 250 µg/mL fungizon. All assays were performed using early passage cells (< 5) harvested from subconfluent monolayers.

Cell Behavior Bioassays. (i) Adhesion assay: Cells were incubated overnight with ^{51}Cr (40 µCi/10^6 cells), washed in Ca^{2+}, Mg^{2+} - free HBSS, and harvested by a 4-minute incubation in 0.05% trypsin, 0.53 mM EDTA in HBSS. The cells were then washed twice with 0.5% BSA in HBSS and resuspended in serum-free modified MCDB 131 (Clonetics Inc.) containing 2% BSA. The test surface was incubated with ^{51}Cr-labeled cells at a concentration of 5 x 10^4 cells/cm^2 for 2 hours at 37 °C. Non-adherent cells were removed by three gentle washes with 0.5% BSA in HBSS and remaining adherent cells solubilized with 1% Triton X-100. Radioactivity was measured in a gamma counter and expressed as percent adherent cells (100 x adherent cells (cpm/cm^2)/total input cells (cpm/cm^2)). (ii) Migration assay: We have adapted microcarrier cell culture methods for the evaluation of EC migration. Endothelial cells were grown to confluence in tissue culture flasks, harvested by collagen microcarrier beads (Cyto cells become confluent on the beac d the beads incubated overnight. resuspended in endothelial growth concentration of 1 x 10^4 cells/cm^2. adherent cells solubilized with 1% We have also used this system to st say: ECs were incubated on the lls were pulsed with ^3H-thymidi rvested with a Tomtec Cell Harv ntrol surfaces included plain gol mean ± standard error (n ≥ 5) ar

RESULTS AND DISCUSSION

Atomic force images of mono surface structures consistent with a 1). At both low and high magnific oblique, and its dimensions are a corresponding to a molecular area obtained using low-angle x-ray diff the formation of a surface bound cr of $GRGD(\beta A)_3YNH(CH_2)_2SH$ coa 250 to 500 Å in diameter, surround to a 1:1 mix of these peptides dem was no evidence of unoccupied gol

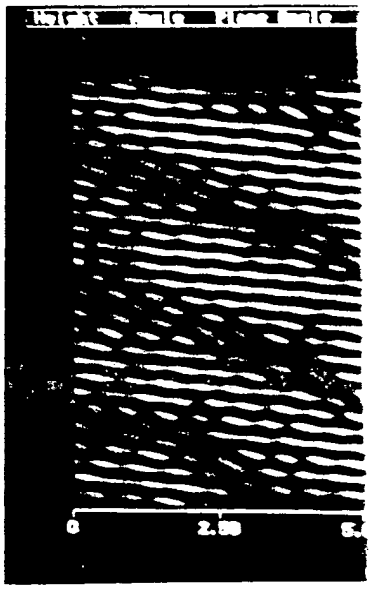


Fig. 1. AFM image of $(\beta A)_6NH$

tissue culture flasks, harvested by trypsinization, and placed in a spinner flask with 25 mg of collagen microcarrier beads (Cytodex 3 beads, Pharmacia Biotech Inc., Piscataway, NJ). After the cells become confluent on the bead surface, ^{51}Cr (40-100 μCi/10^6 cells) is added to the medium and the beads incubated overnight. The beads were then washed in Ca^{2+}, Mg^{2+} - free HBSS, resuspended in endothelial growth medium (EGM), and plated onto the test surface at a concentration of 1×10^4 cells/cm^2. After a 48-hour incubation period, the beads are removed, adherent cells solubilized with 1% Triton X-100, and radioactivity measured in a gamma counter. We have also used this system to study cell migration in a co-culture environment.(iii) Proliferation assay: ECs were incubated on the test surface in EGM for 48 hours. During the last 16 hours, cells were pulsed with ^3H-thymidine. Cells were then washed twice in Ca^{2+}, Mg^{2+} - free HBSS, harvested with a Tomtec Cell Harvester, and radioactivity counted in a liquid scintillation counter. Control surfaces included plain gold on glass and 1% gelatin. Data from all assays are expressed as mean ± standard error ($n \geq 5$) and statistical analysis performed using a student's t-test.

RESULTS AND DISCUSSION

Atomic force images of monolayers of $(\beta A)_6NH(CH_2)_2SH$ demonstrated highly aligned surface structures consistent with a homogenous, self-assembled, close-packed monolayer (Fig. 1). At both low and high magnification the surface was free of defect sites. The surface unit cell is oblique, and its dimensions are a = 5.85 ± 0.77 Å, b = 3.60 ± 0.31 Å, θ = 48.17 ± 3.01, corresponding to a molecular area of 15.69 ± 1.36 Å^2. The unit cell area is similar to values obtained using low-angle x-ray diffraction techniques for β-pleated forming peptides and suggests the formation of a surface bound crystalline, parallel β-sheet monolayer structure [2]. AFM scans of $GRGD(\beta A)_3YNH(CH_2)_2SH$ coated surfaces revealed protein islands, measuring approximately 250 to 500 Å in diameter, surrounded by unoccupied Au-coated mica (Fig. 2). Substrates exposed to a 1:1 mix of these peptides demonstrated combined features of both surfaces. However, there was no evidence of unoccupied gold. AFM was not performed on BSA treated films.

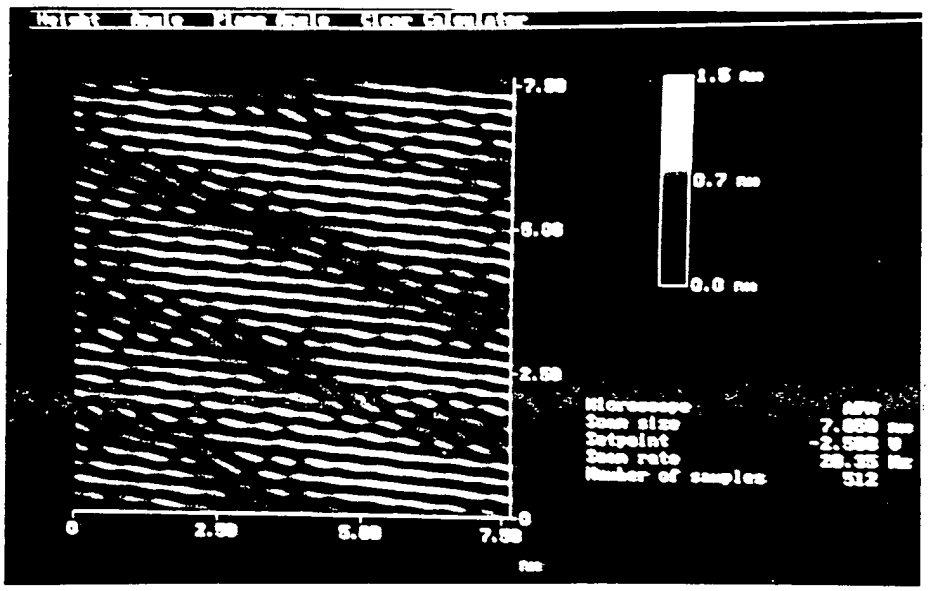


Fig. 1. AFM image of $(\beta A)_6NH(CH_2)_2SH$ self-assembled monolayer on Au/mica

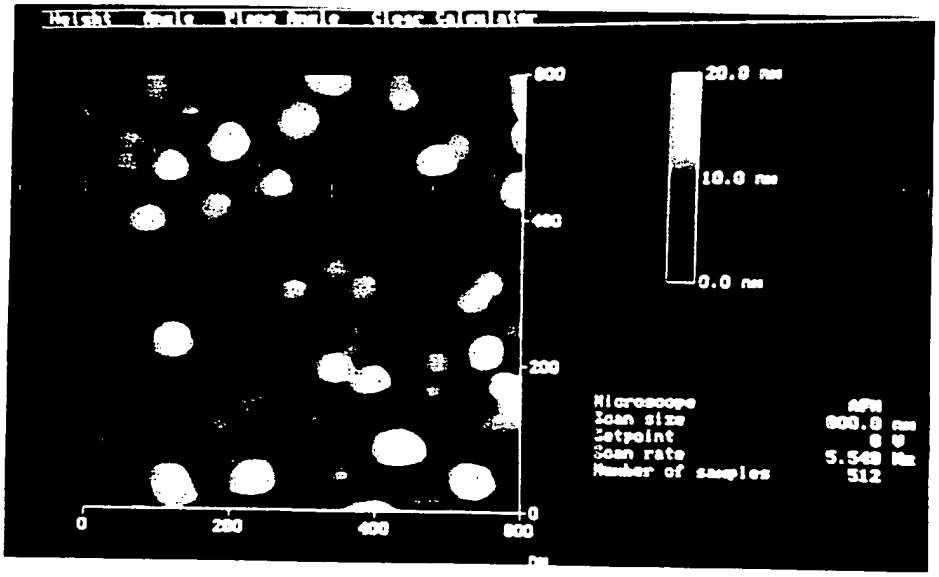


Fig. 2. AFM image of GRGD$(\beta A)_3$YNH$(CH_2)_2$SH self-assembled monolayer on Au/mica

External reflectance infrared spectra in the 1400 to 1900 cm^{-1} range demonstrate characteristic amide I and II bands (Fig. 3). These bands have approximately opposite dichroic properties which has been useful for determining qualitatively, the orientation of peptide films [4, 5]. In principle, the intensity of the amide I band exceeds that of the amide II spectral band for perpendicularly oriented films when the IR spectra are obtained with p-polarized light. For the self-assembled monolayer of $(\beta A)_6$NH $(CH_2)_2$SH, the dominant amide II band suggests a significant tilt of the chain axis with respect to the surface normal.

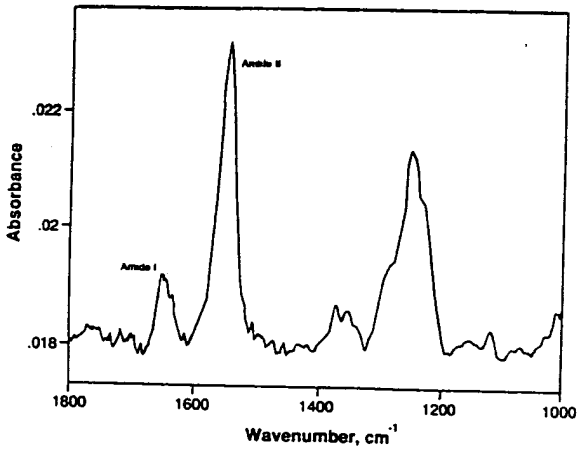


Fig. 3. Infrared spectra of $(\beta A)_6$NH $(CH_2)_2$SH (A) and GRGD$(\beta A)_3$YNH$(CH_2)_2$SH (B).

The presence of peaks at 1630 and
presence of β-sheet structure. It w
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Cell adhesion, migration, and
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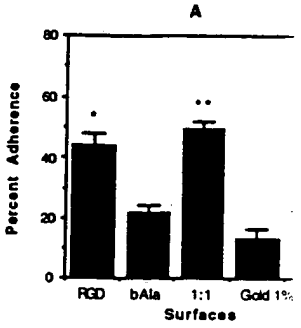


Fig. 4. EC adhesive (A) and proli
βAla or Gold; **p < 0.005 1:1 vs β.

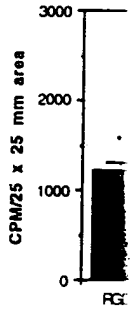
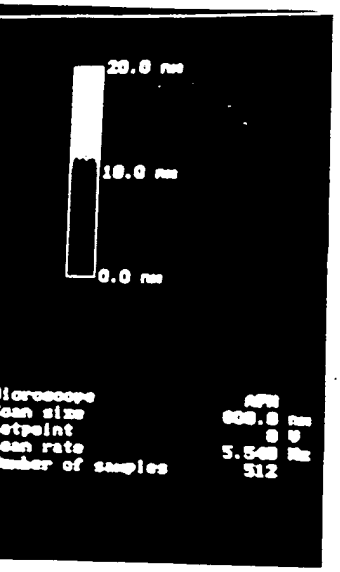


Fig. 4C. EC migration re

CONCLUSIONS

Protein self-assembly is based l
pleated architecture which suggests a
monolayers with the potential for bo
Specifically, we have determined tha



mbled monolayer on Au/mica

range demonstrate characteristic
pposite dichroic properties which
ptide films [4, 5]. In principle,
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ggests a significant tilt of the

$(\beta A)_3YNH(CH_2)_2SH$ (**B**).

The presence of peaks at 1630 and 1670 cm^{-1} for all observed peptide coated substrates indicate the presence of β-sheet structure. It was not possibly to quantify the exact angle of tilt or the extent of β-sheet architecture using this methodology.

Cell adhesion, migration, and proliferation responses are illustrated in Figure 4 (a, b, c). Responses were significantly higher on surfaces coated with the integrin ligand $GRGD(\beta A)_3YNH(CH_2)_2SH$ compared with observed cell behavior on βAla surfaces or gold. Quantitation of the amount of surface adsorbed peptide was not performed in these studies.

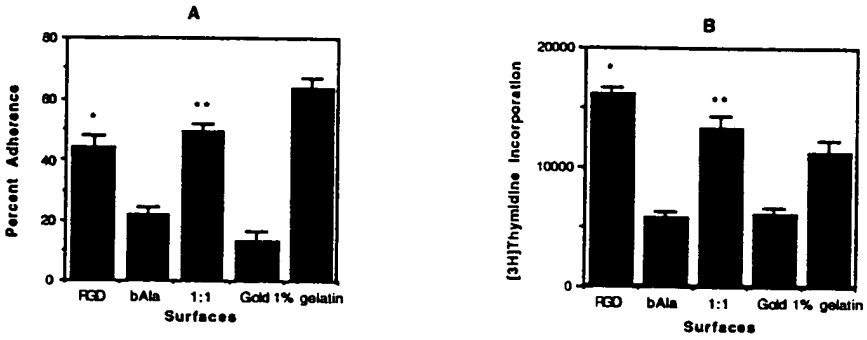

Fig. 4. EC adhesive (A) and proliferative (B) behavior on test substrates (*p < 0.005 RGD vs βAla or Gold; **p < 0.005 1:1 vs βAla or Gold). All surfaces pretreated with BSA.

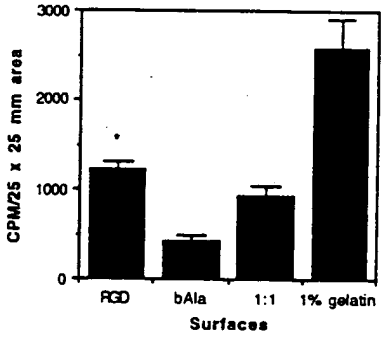

Fig. 4C. EC migration responses on test substrates (*p < 0.005 RGD vs βAla).

CONCLUSIONS

Protein self-assembly is based largely on H-bonding interactions and the formation of β-pleated architecture which suggests a new paradigm for creating close-packed, self-assembling monolayers with the potential for both enhanced physiochemical and biological properties. Specifically, we have determined that poly(βalanine)thiolates on gold self-assemble as uniform

monolayers. Appropriately tailored primary amino acid sequences as pendant structures modulate receptor mediated cell behavior. Current work is directed at examining film biostability, anti-parallel packing, and the effects on monolayer morphology of pendant group size to poly(βalanine) chain length.

ACKNOWLEDGMENTS

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ELECTRIC
BIOACTIVE POLYPE

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ABSTRACT

We have developed proces
of protein polymers on a variety o
biocompatible coatings on silicon
research has identified several can
significant 0.1 to 100 micrometer l
able to process polypeptides into b
of the structural evolution of the co
strength and geometry or solution
neurons and glial cells are examine
microscopy, atomic force microsc
microscopy provide insight about t
their macroscopic properties.

INTRODUCTION

Materials scientists are cons
tune physical properties toward a sp
molecular engineers to design preci
previously unknown in nature. The
appropriate processing schemes to
study are genetically engineered to
occurring extracellular matrix prote
to provide structural integrity. The
to the target cells and the structural s
stable oriented crystalline domains.
fiber formation, produces fibrous ne
50 nanometers. These tiny filament
area-to-volume ratio.

Three-Dimensionally Tailored Films

The fibrous, nonwoven netw
example of structures that can be des
dimensionally tailored film or coatin
thickness over a length scale that is
relevant length scale is 0.1 to 100 mi
biological applications are porosity,
timed drug release. Gradients in por
the density of coating elements, such
porosity allows for control over the e
well as governing transport through t
soft, living tissue (modulus ~10 MPa
perhaps be accommodated by a gradi